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09/581,861	03/05/2001	James R. Broach	60623(50370)	4402
21874 7590 02/03/2009 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER				
LIU, SUE XU				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/581,861

Applicant(s)

BROACH ET AL.

Examiner

SUE LIU

Art Unit

1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 53, 54, 57, 59, 60 and 120-122 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 53, 54, 57, 59, 60 and 120-122 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/19/08 has been entered.

Status of the Claims

2. Claims 2-52, 55-56, 58, 61-119 and 123-131 have been canceled as filed on 6/19/08.
Claims 1, 53, 54, 57, 59, 60, and 120-122 are presently pending.
Claims 1, 53, 54, 57, 59, 60, and 120-122 are being examined in this application.

Election/Restrictions

3. Applicant's election of the "single disclosed species" of the human bradykinin receptor as the heterologous G protein coupled receptor and the sandwich chimera Galphaq(1-11)-GPA1 (6-467)-Galpaq(355-359) of Example 12, which substitutes both the N and C terminus of GPA1 with 1st and 2nd heterologous subunits derived from the same source, in the reply filed on 8/20/04 is as previously acknowledged.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The present application (09/581,861 filed 3/5/2001) claims priority under:

- a. 371 of PCT/US98/21168 (filed 10/07/98); and
- b. CIP of 08/946,298 (filed 10/7/97) as well as earlier applications.

Upon review of the two above cited documents, the presently claimed (and elected invention) finds disclosure support in the PCT/US98/21168 application (filed 10/07/98) BUT not the 08/946,298 (filed 10/7/97) application which lacks direct or exemplary support for the presently claimed scope of claims e.g. the substitution GPA variants as well as the sandwich chimeras. Accordingly, the present elected claims are granted the filing date of the PCT application (e.g. 10/7/98) for purposes of prior art.

Specification

5. Applicant's amendments to the specification to update the continuation data and to recite the corresponding SEQ ID NOs in the "BRIEF DESCRIPTION OF THE FIGURES AND TABLES" of the instant specification (filed on 6/19/2008) is acknowledged and entered.

Claim Objection(s) / Rejection(s) Withdrawn

6. In light of applicants' amendments to the claims and upon further consideration, the following rejections as set forth in the previous office action are withdrawn:

A.) Claims 1, 59, 121 and 122 are rejected under 35 U.S.C. 102(b) as being anticipated by Pausch et al. WO 95/21925 (8/95 ; cited in previous Office action mailed on 10/19/2004).

B.) Claims 1, 53, 59, and 120-122 are rejected under 35 U.S.C. 102(b) as being anticipated by Fowlkes et al. WO 94/23025(10/94; cited in previous an Office action mailed on 10/19/2004).

C.) Claims 1, 53, 54, 57, 59, 60, and 120-122 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

D.) Claims 1, 53, 54, 57, 59, 60, and 120-122 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for generating recombinant yeast cells comprising certain heterologous G-protein coupled receptors (GPCR) (e.g. C5a, FPRL, ML1aR etc.; p.91 and 104 of the instant specification) with certain GPA1 chimeric G-protein subunit, does not reasonably provide enablement for any combination of GPCR and mutant G-protein alpha subunit within any recombinant yeast cell.

E.) Claim 1, 53, 59 and 120-122 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,864,060 in view of Fowlkes et al (WO 94/23025; 10/94).

7. In light of applicant's amendment to the claims, and in order to clarify the records, the following claim rejections are withdrawn:

A.) Claims 1, 57, 59, 121 and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pausch et al WO 95/21925 (8/95 ; cited previously) and Conklin et al (Molecular Pharmacology, Vol. 50(4) Oct. 1996 pages 885-890; cited previously).

B.) Claims 1, 53, 57, 59, and 120-122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pausch et al WO 95/21925 (8/95) and Conklin et al (Molecular Pharmacology, Vol. 50(4) Oct. 1996 pages 885-890) as applied to claims 1, 57, 59, 121 and 122 above, and further in view of Fowlkes et al. WO 94/23025(10/94).

C.) Claims 1, 53, 57, 59, and 120-122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fowlkes et al (WO 94/23025; 10/94) and Conklin et al (Molecular Pharmacology, Vol. 50(4) Oct. 1996 pages 885-890).

D.) Claims 1, 53, 54, 57, 59, 60, and 120-122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pausch et al (WO 95/21925; 8/95), Fowlkes et al (WO 94/23025; 10/94), and Conklin et al (Molecular Pharmacology, Vol. 50(4) Oct. 1996 pages 885-890) as applied to claims 1, 53, 57, 59, and 120-122 above, and further in view of Hamm, (J. Biol. Chem., Vol. 273(2) (Jan. 1998) pages 669-672).

New Claim Rejections

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Fowlkes and Others

9. Claims 1, 53, 54, 57, 59, 60, and 120-122 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Fowlkes** et al (WO 94/23025; 10/94; cited previously), **Pausch** et al WO 95/21925 (8/95; cited previously), **Conklin** et al (Molecular Pharmacology, Vol. 50(4) Oct. 1996 pages 885-890; cited previously), and **Hamm**, (J. Biol. Chem., Vol. 273(2) (Jan. 1998) pages 669-672; cited previously), and if necessary, further in view of **Lambright** et al (Nature. Vol. 379:311-319; 1996; cited previously). The previous rejection is maintained for the reasons of record as set forth in previous Office actions as well as for the reasons below.

Fowlkes et al, throughout the reference, teach "chimeric G-Protein subunits" comprising a chimeric G-protein subunit comprising the yeast G alpha unit (e.g. GPA1) in which at least 10, 20 or 40 (only final 10 or 20 deemed critical: see page 43-top of page 44) of the yeast's C-

terminal amino acids are substituted by with a substantially homologous mammalian (or other exogenous) C-terminal amino acids $G\alpha$, which reads on the chimeric G-protein of **clms 1 and 53**.

The reference also teaches the yeast cell comprising:

A. a heterologous G-protein coupled receptor (GPCR) which acts as a surrogate for an endogenous yeast pheromone receptor in a pheromone response pathway of the yeast cell (e.g. Abstract and p. 12, para 2, p.14, para 4-5 of the reference), which reads on the heterologous G-protein coupled receptor of **clms 1 and 53**; and

B. the above “chimeric G-Protein subunits” such that expression of the chimeric G-protein subunit functionally integrates said heterologous GPCR into the pheromone response pathway of the yeast cell and wherein modulation of the signal transduction activity of the heterologous GPCR by an extracellular signal provides a detectable signal. E.g. see Fowlkes et al. Abstract; pages 7-9; pages 12-17; page 23-25; pages 37-40; pages 43-44, particularly bottom of page 43-top of page 44; examples and claims 1-37 (especially for example claims 1, 28 and 29).

The reference also teaches the chimeric $G\alpha$ subunit “in which a portion, e.g., at least about 20 or preferably at least about 40, amino acids, which is substantially homologous with the corresponding residues of the amino terminus of the yeast $G\alpha$, is fused to a sequence substantially homologous with the main body of a mammalian $G\alpha$ ” (bridging para of p. 43-44). In other words, the amino-terminal of the chimeric $G\alpha$ subunit (at least 20 amino acids) is “substantially homologous” with the yeast $G\alpha$. The reference also defines the term “substantially homologous” as “at least 50%, more preferably at least 80%, identical in sequence” (p. 23, lines

25+ of the reference). Taking together, for example, an amino-terminal with a 20 amino acid residues would comprise 10 to 16 yeast $G\alpha$ amino acid residues at the N-terminus of the chimeric $G\alpha$ subunit. Thus, the reference teaches at least replacing a number (such as in the range of 1-11) of amino acids at the N-terminus or linking amino acid residues to the N-terminus, as recited in **clms 53 and 1** respectively.

The reference also teaches inactivation of endogenous pheromone receptor proteins of yeast cells (p. 55, lines 10+), which reads on the pheromone receptor not produced in functional form of **clm 120**. The reference also teaches that in order to achieve selection or screening, the yeast must have an appropriate phenotype, and host yeast cells having native proteins that are being surrogated would frustrate the genetic selection process (p. 55, lines 10+). Thus, a person of ordinary skill in the art would have been motivated at the time of the invention to inactivate an endogenous G-protein receptor (a pheromone receptor), because the in activation is necessary to carry out the intended screening or step when using a heterologous receptor as a surrogate for the endogenous receptor, as taught by Fowlkes et al.

The reference also teaches integrating reporter construct into the host yeast cells (bridging para p. 17-18), which reads on the indicator gene of **clm 121**.

The reference also teaches that the host yeast cell are *Saccharomyces cerevisiae* (e.g. p. 54, lines 15+), which reads on the yeast cell of **clm 122**.

Fowlkes et al do not explicitly teach substituting between the last 4-6 of C-terminal amino acids (e.g. four amino acids) of GPA1 or substitution of the last five (5) C-terminal GPA1 amino acids, as recited in **clms 1, 53, 54 and 57**. The Pausch reference also does not explicitly

teach replacing 1-11 (or 4 to 6, or 5) of the first N-terminal amino acids of GP α 1 as recited in **clms 1, 53, 54, 59 and 60**.

However, **Pausch**, throughout the reference, teaches yeast cells transformed with nucleic acids that encode heterologous G protein coupled receptors (Abstract, Claims 1-29, pp. 3-5, pp. 13-14, pp. 19-24, and Examples of the reference). The reference also teaches the recombinant yeast cells comprising “chimeric G-Protein subunits” comprising GPA1 and G α in which the chimeric is formed by fusing the amino terminal domain of yeast GPA1 and the carboxy terminal domain of a heterologous G α (pp. 14, lines 17-20, and Claims 17 and 18 of the reference). The reference also teaches that the chimeric G protein can be all or a portion of a G protein $\alpha\beta\gamma$ complex (p. 3, lines 24+), and the yeast G α subunit (i.e. Gpa1) is to be associated with heterologous G $\beta\gamma$ subunits (p. 14, lines 4+ and 21+).

Pausch also teaches that (p. 14 of the Pausch reference):

- a. the “carboxyl terminal domain” of GPA1 can be substituted by the carboxyl terminal domain of a heterologous Galpha; and
- b. that “One can easily determine which configuration is best suited for adequate coupling to a particular heterologous receptor by simply constructing vectors as taught herein and measuring the signaling of ligand binding in response to a given assay”

Accordingly, it would be obvious to one of ordinary skill in the art at the time of applicant’s invention to determine optimum minimum C-terminal GPA1 length necessary to obtain coupling as well as additional amino acids encompassing such a minimum number (e.g. 5, 6 ... entire C-terminus) for a particular heterologous receptor.

Alternatively, in this regard, the **Conklin** reference provides evidence that substitution of “at least four C-terminal” Galpha amino acids are necessary (e.g. both -3 and -4 positions) in order to permit coupling to a new receptor (e.g. heterologous receptor). See e.g. Abstract and data obtained therein.

Thus, in light of the Conklin reference teaching, the selection of “last 4-6 C-terminal amino acids of said GPA1” or 5 amino acids, for substitution with the corresponding C-terminal heterologous Galpha would have been obvious to one of ordinary skill in the art at the time of applicant’s invention in order to obtain coupling to a particular heterologous receptor.

A person of ordinary skill in the art would have been motivated at the time of the invention to substitute the desired number of C-terminal residues such as five residues, because Pausch teaches the need to optimize chimeric G-protein subunit by mutating (or substituting) certain numbers of amino acid residues at the C-terminus, and Conklin reference teaches specific number of mutations (such as five residues) at the C-terminus would allow binding to a heterologous receptor as discussed above.

In addition, **Hamm** teaches the structure and role of the G protein heterotrimer; particularly the different Galpha subunits and their corresponding receptors (e.g. including bradykinin: see page 669; page 670, right column). The Hamm reference teaches that in addition to the C-terminus of G protein alpha subunits being critical in determining receptor-G protein specificity (as discussed in the above Pausch, Fowlkes, and Conklin references), the N-terminus of the alpha G-protein subunit also appears to be involved in promoting heterologous receptor contact or coupling. E.g. see Abstract; page 669, especially right column; the figures, especially

figures 1 and 2, but particularly figure 2 and the role of the 1st N-terminal 23 amino acids of Galpha and rhodopsin receptor)

Accordingly, the Hamm reference would provide motivation to one of ordinary skill in the art at the time of applicant's invention to further modify the chimeric Galpha protein subunits obtained by the Pausch, Fowlkes, and Conklin references by linking or substituting into the N terminal portion of the reference chimeras corresponding heterologous amino acids in order to obtain sandwich chimeras (e.g. N-term heterologous-GPA1-C terminal heterologous) that can be screened for different degrees (e.g. increased/decreased) of heterologous receptor coupling.

The determination of the optimum number of N-terminally linked or substituted heterologous amino acids (e.g. at least 5; i.e. 11) with regard to a particular heterologous receptor and corresponding chimera construct was well within the skill of the art utilizing art-recognized screening techniques. E.g. see Pausch, Fowlkes, and Conklin references and assays disclosed therein.

Further, **Lambright** et al, throughout the publication, teach various G protein α subunits as well as comparison of the amino acid sequences (e.g. Abstract). The reference teaches that the N-terminal amino acid residues among the various G protein α subunits are conserved with homologous sequences (e.g. p.313). As indicated in Figure 1 of the reference, the first few amino acid sequences are highly conserved (such as the first three amino acids).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to additionally modify the N-terminus portion of GPA1 of the Pausch, Fowlkes, and Conklin references to replace the first 1-11 N-terminal amino acids with the 1st 11 N-terminal amino acids of a heterologous G protein subunit and arrive at the presently claimed

sandwich chimeras with a reasonable expectation of success of obtaining modified chimeras which possessed varying degrees (e.g. increased/decreased) of heterologous receptor coupling for use in screening assays (e.g. receptor agonists/antagonists).

A person of ordinary skill in the art would have been motivated at the time of the invention to design an appropriate chimeric G-protein subunit comprising the necessary mutations such as 5 amino acid substitution at the N-terminus, because Fowlkes et al teach the need to design heterologous G-protein subunit that is compatible with the expressed heterologous G-protein coupled receptor. In addition, because the cited references (such as Fowlkes, Hamm and Lambright) teach making N-terminal mutations in G protein α subunits to generate GPCR compatible GPA subunits, it would have been obvious to one skilled in the art to substitute one number of amino acid mutations at the N-terminus for the other to achieve the predictable result of generating heterologous GPCR compatible G protein α subunits.

An ordinary skilled artisan would have reasonable expectation of success of achieving such modifications because the techniques for generating such recombinant yeast cells comprising the desired heterologous receptor and chimeric G-protein subunits are known and routine in the art as taught by the cited references.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in *italic*):

Only the relevant arguments regarding the previously cited references are discussed below.

Applicants seem to argue that the cited references (Pausch, Conklin, Fowlkes and Hamm) do not teach all elements, and/or the said references do not provide motivation to combine. (Reply, pp. 16+).

In responds to applicant's argument that the references do not teach all elements, applicants are respectively referred to the above rejection for detailed discussion.

In response to applicants' argument that there is no motivation to combine all the references, applicants' are directed to the above discussion and the reasons of record for reasons to combine the cited references, especially for mutations of the G-protein subunits in both of the N- and C-terminus.

Furthermore, applicants are also respectfully directed to the recent Supreme Court decision, which forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR, 127 S.Ct. at 1741, 82 USPQ2d at 1396.*

Specifically, applicants also argue that the Hamm reference does not provide motivation to modify the N-terminus of Gpa1. As discussed in the previous rejection (Office action, 8/24/06, pp. 25+), the Hamm reference specifically teaches that the N-terminal regions of the alpha subunit along with the C-terminal region of the gamma subunit are both sites of lipid modification suggesting *a site of membrane attachment* (e.g. emphasis provided: see Hamm p. 669, right column 2nd full paragraph). Additionally evidence provided by references cited by Hamm leads to the conclusion by the Hamm reference that "A larger region of the C-terminal region of the Galpha subunits, as well as the N-terminal helix, has been *implicated in receptor*

contact "(emphasis provided: See Hamm p. 669, right column, penultimate paragraph). Accordingly, in contradistinction to applicant's argument, the Hamm reference does specifically teach and/or suggest that the N-terminus of G protein alpha subunits is critical to promoting heterologous receptor contact or coupling.

Applicant further argues that the Hamm reference teaches away from modifying the N-terminus.

The Examiner respectfully disagrees.

Additionally, as pointed out in the previous set forth rejection, the Hamm reference teaches and/or suggests that the N-terminus of the alpha G-protein alpha subunit is involved in promoting heterologous receptor contact or coupling. E.g. see Abstract; page 669, especially right column; the figures, especially figures 1 and 2. More particularly the reference points to the role of the 1st N-terminal 23 amino acids of the G-protein alpha subunit. See e.g. Figure 1, but particularly figure 2 and the role of the 1st N-terminal 23 amino acids of Galpha and rhodopsin receptor.

Accordingly, applicant's claims broadly encompass operably linking and/or substituting 5 or more (e.g. the entire N-terminus) amino acids of the N-terminus. In this respect, the reference provides guidance as to linking and/or substituting of 1 or more N-terminal amino acids up to the 23rd amino acid.

In the present instance, although the Hamm reference states that the C-terminus of the alpha subunit is the best characterized receptor contact region, the reference nevertheless provides evidence (as discussed above) that implicates the N-terminus in receptor contact and membrane attachment. Accordingly, the Hamm reference provides motivation to one of ordinary

skill in the art to modify the N-terminus of alpha G-protein subunit in a manner analogous to that performed on the C-terminus in accordance with the Pausch et al, Fowlkes et al, and Conklin references with a reasonable expectation of making a yeast cell comprising a chimeric G-protein subunit and heterologous G-protein-coupled receptor which act as a "surrogate for an endogenous yeast pheromone receptor in a pheromone response pathway of the yeast cell .

Further, Lambright et al, throughout the publication, teach various G protein α subunits as well as comparison of the amino acid sequences (e.g. Abstract). The reference teaches that the N-terminal amino acid residues among the various G protein α subunits are conserved with homologous sequences (e.g. p.313). As indicated in Figure 1 of the reference, the first few amino acid sequences are highly conserved (such as the first three amino acids).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to additionally modify the N-terminus portion of GPA1 of the Pausch, Fowlkes, and Conklin references to replace the first 1-11 N-terminal amino acids with the 1st 11 N-terminal amino acids of a heterologous G protein subunit and arrive at the presently claimed sandwich chimeras with a reasonable expectation of success of obtaining modified chimeras which possessed varying degrees (e.g. increased/decreased) of heterologous receptor coupling for use in screening assays (e.g. receptor agonists/antagonists).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SUE LIU/
Patent Examiner, Art Unit 1639
1/16/09